AF$

Docket: A-1789div

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Pandian et al.

U.S. Serial No: 10/716,739

Filed: 11/18/03

For: METHODS AND KITS FOR DETECTING ITA IN A BIOLOGICAL SAMPLE

Examiner: Gary W. Counts

Group Art: 1641

ATTENTION: Board of Patent Appeals and Interferences

CERTIFICATE OF MAILING (37 CFR 1.8a)
I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to:
Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Signed: Jennifer K. Rosenfield

Date: 12/22/06
December 22, 2006

TRANSMITTAL OF APPEAL BRIEF (PATENT APPLICATION -- 37 CFR 1.193)

1. Transmittal herewith in triplicate is the APPEAL BRIEF in this application with respect to the Notice of Appeal filed on **August 22, 2006.**

2. **STATUS OF APPLICANT**

This application is on behalf of

[X] other than a small entity

[ ] small entity

verified statement:

[ ] attached

[ ] already filed

3. **FEE FOR FILING APPEAL BRIEF**

Pursuant to 37 CFR 1.17(f) the fee for filing the Appeal Brief is:

[ ] small entity	$ 250.00
[X] other than a small entity	$ 500.00

Appeal Brief fee due

$ 500.00

4. EXTENSION OF TERM

The proceedings herein are for a patent application and the provisions of 37 CFR 1.136 apply.

(complete (a) or (b) as applicable)

(a) [X] Applicant petitions for an extension of time under 37 CFR 1.136 (fees: 37 CFR 1.17(a)-(d)) for the total number of months checked below:

	Extension (months)	Fee for other than small entity	Fee for small entity
[ ]	one month	**$120.00**	$60.00
[X]	two months	$450.00	$225.00
[ ]	three months	$1020.00	$510.00
[ ]	four months	$1590.00	$795.00

If additional extension of time is required please consider this a petition therefor.

(check and complete the next item, if applicable)

[ ] An extension for _____ months has already been secured and the fee paid therefor of $ _____ is deducted from the total fee due for the total months of extension new requested.

Extension fee due with this request $ 450.00

or

(b) [ ] Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

4. TOTAL FEE DUE

The total fee due is:

Appeal brief fee $ 500.00

Extension fee (if any) $ 450.00

TOTAL FEE DUE $ 950.00

5. FEE PAYMENT

[ ] Attached is a check equaling the sum of **$ 0.00**

[X] Charge Account Number **13-5135** the sum of $ 950.00
A duplicate of this transmittal is attached.

Docket: A-1789div

6. FEE DEFICIENCY

[X] If any additional extension and/or fee is required, this is a request therefor and to charge Account Number **13-5135**.

AND/OR

[X] If any additional fee for claims is required, charge Account Number **13-5135**.

Respectfully submitted,

Jennifer K. Rosenfield
Registration Number **53,531**

Stout, Uxa, Buyan & Mullins, LLP
4 Venture, Suite 300
Irvine, CA 92618

phone: 949-450-1750
fax: 949-450-1764

12/22/06

Docket Number: A-1789div

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Pandian et al.	/	Confirmation No.: 6774
Serial No: 10/716,739	/	Group Art Unit: 1641
Filed: 11/18/03	/	Examiner: Gary W. Counts
For: METHODS AND KITS FOR DETECTING ITA IN A BIOLOGICAL SAMPLE	/	Customer No.: 33197

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANT'S BRIEF (37 CFR §41.37)

Sir:

This brief is in furtherance of the Notice of Appeal filed in this case on August 22, 2006. A transmittal letter, including a Certificate of Mailing, accompanies this brief.

REAL PARTY IN INTEREST (37 CFR §41.37(c)(1)(i))

The assignee of record is the real party in interest.

RELATED APPEALS AND INTERFERENCES (37 CFR §41.37(c)(1)(ii))

There are no related appeals or interferences previously or currently pending.

STATUS OF CLAIMS (37 CFR §41.37(c)(1)(iii))

The application on appeal, as filed, contained 41 claims, of which claims 1, 19, 23, 26, and 35 were independent. Dependent claims 42-44 have been subsequently added by

amendment. Presently, claims 23-25 and 42-44 stand rejected, having been finally rejected on May 18, 2006. No claims stand allowed. Thus, the status of the claims is as follows:

cancelled claims – 38

allowed claims -- None

claims objected to -- None

claims rejected -- 23-25 and 42-44

claims withdrawn -- None

The claims on appeal are Claims 23-24 and 42-44.

STATUS OF AMENDMENTS (37 CFR §41.37(c)(1)(iv))

A preliminary amendment was filed with the application on November 18, 2003, which was entered. An amendment was filed on September 30, 2004, which was entered. An election in response to a restriction requirement was made on January 10, 2005 with traverse. The election with traversal was acknowledged, but the restriction requirement was deemed proper. An amendment was filed on June 6, 2005, which was entered. An amendment was filed February 23, 2006, which was entered. An amendment was filed July 18, 2006, which was entered. No other amendments have been filed or entered. The foregoing section listing the present status of the claims takes into account all amendments of record.

SUMMARY OF CLAIMED SUBJECT MATTER (37 CFR §41.37(c)(1)(v))

The subject matter of the present claims comprises a method for detecting a trophoblastic disease in a subject comprising the steps of: contacting a biological sample obtained from a subject with a first antibody that specifically binds hyperglycosylated human chorionic gonadotropin and a different second antibody that specifically binds human chorionic gonadotropin, in one assay; determining an amount of hyperglycosylated human chorionic

gonadotropin present in the biological sample; determining an amount of human chorionic gonadotropin present in the biological sample; confirming that the subject is not pregnant; comparing the determined amount of hyperglycosylated human chorionic gonadotropin present in the sample to a 50th percentile of amounts of hyperglycosylated human chorionic gonadotropin present in samples obtained from subjects who do not have a trophoblastic disease; and comparing the determined amount of human chorionic gonadotropin present in the sample to a 50th percentile of amounts of human chorionic gonadotropin present in samples obtained from subjects who do not have a trophoblastic disease, wherein an amount of hyperglycosylated human chorionic gonadotropin and an amount of human chorionic gonadotropin present in the sample which is greater than the 50th percentile of the amounts of hyperglycosylated human chorionic gonadotropin and human chorionic gonadotropin present in the samples obtained from subjects who do not have a trophoblastic disease, respectively, indicates the presence of a trophoblastic disease.

The

trophoblastic disease is may be choriocarcinoma. The sample may be liquid samples or tissue samples. The determining step may comprise detecting a signal produced by a label (e.g., a chemiluminescent signal).

For the convenient reference of the Board, a copy of the claims on appeal is presented in Appendix A.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL (37 CFR §41.37(c)(1)(vi))

Claims 23-25 and 42-44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cole et al. (Clinical Chemistry Feb 2001; hereinafter Cole) in view of O'Connor et al. (U.S. 6,500,627; hereinafter O'Connor) in light of Birken et al. (2001; hereinafter Birken 2001) in view of Hochstrasser et al. (US 2003/0157580; hereinafter Hochstrasser) and Birken et al. (US 6,521,416; hereinafter Birken '416). Claim 44 was also rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Cole in view of O'Connor in light of Birken 2001 in view of

Hochstrasser and Birken '416, and further in view of Campbell et al. (US 4,946,958; hereinafter Campbell).

ARGUMENT (37 CFR §41.37(c)(1)(vii))

The Examiner rejected claims 23-25 and 42-44 under 35 U.S.C. § 103(a) as being unpatentable over Cole et al. (Clinical Chemistry Feb 2001; hereinafter Cole) in view of O'Connor et al. (U.S. 6,500,627; hereinafter O'Connor) in light of Birken et al. (2001; hereinafter Birken 2001) in view of Hochstrasser et al. (US 2003/0157580; hereinafter Hochstrasser) and Birken et al. (US 6,521,416; hereinafter Birken '416). Claim 44 was also rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Cole in view of O'Connor in light of Birken 2001 in view of Hochstrasser and Birken '416, and further in view of Campbell et al. (US 4,946,958; hereinafter Campbell).

According to the final rejection of May 18, 2006, it would have been obvious to one of skill in the art to incorporate antibodies and labels as taught by O'Connor et al. into the method of diagnosing as taught by Cole et al. The Examiner relies on Cole as teaching that patients can be diagnosed with choriocarcinoma solely from a persistent positive hCG result, in the absence of pregnancy, but that Cole is generic with respect to the reagents used in the immunoassay. The Examiner states that Cole fails to specifically state the use of antibodies to the hyperglycosylated hCG and also fails to use labels in the immunoassay. The Examiner relies on O'Connor to teach that hyperglycosylated hCG and hCG are elevated in trophoblastic disease, and the use of antibodies to hyperglycosylated hCG and hCG in an assay to diagnose gestational trophoblastic disease.

Appellants respectfully traverse the rejections. Appellant's claims are directed to a diagnostic method that uses two different antibodies, "a first antibody that specifically binds hyperglycosylated human chorionic gonadotropin" and "a different second antibody that specifically binds human chorionic gonadotropin". The two antibodies are detected and compared to the levels of hyperglycosylated hCG and hCG, respectively, in subjects who do not have trophoblastic disease.

The Examiner relies on O'Connor as teaching the use of two different antibodies in immunoassays in the diagnosing of trophoblastic disease, specifically B152, an antibody to hyperglycosylated hCG, and B108 or B109 as a second hCG-specific antibody. However, unlike in the present claims, the immunoassays in O'Connor teach diagnosing trophoblastic disease based on the measurement of the **ratio** between the hCG forms detected by the first and second antibodies over time (column 9, lines 35-62; Example 4, columns 25-26).

Because it is the ratio of the levels of the two antibodies to each other in O'Connor that serves as the diagnostic criterion for trophoblastic disease, one of skill in the art would not be motivated to use those same antibodies and labels of O'Connor in the method of diagnosing as taught by Cole to arrive at the currently pending claims, which measure the amounts of hCG detected by each antibody, and compares them to the corresponding amounts in subjects without trophoblastic disease. That is, it is the ratio of the two antibodies in O'Connor that is important, and one of skill in the art would not be motivated to use the same antibodies in the methods of Cole in a manner that did not involve measuring the ratio between them, as required by the currently pending claims.

In the final rejection of May 18, 2005, the Examiner asserts that "O'Connor et al. disclose that the amount of B152 isorform (hyperglycosylated hCG) and hCG are increased in trophoblastic disease (col 25-26)." Appellant respectfully disagrees. What O'Connor actually discloses in the cited section is that "[i]n normal pregnancy, the ratio of B152/B109 of the two isoforms of hCG rapidly decreases, eventually inverting. In gestational trophoblast disease including choriocarcinoma or hydatiform mole, the ratio is initially higher than found in normal pregnancy, but does not diminish during the course of the apparent pregnancy." (The next paragraph of the cited passage talks about increased hCG levels, but only in other pregnancy disorders, not trophoblast diseases.) Contrary to the Examiner's assertion, O'Connor does not disclose that the amount of B152 isoform and hCG are increased in trophoblast disease, but only that their ratio to each other is altered.

Additionally, as set forth in Example 3 of the instant application (page 27 of the specification as originally filed), the "combo" assay using an antibody to hyperglosylated hCG (B152) and an antibody to free beta hCG (827) yields unexpected results, in that the combo assay

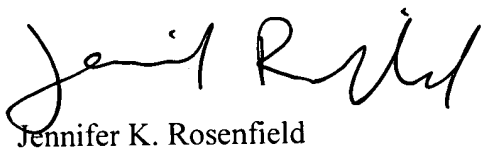
provided about "6 to 12 times greater sensitivity" than the assay using only the B152 antibody (the B152-B207 assay; B207 was the antibody used for detection).

Surprising or unexpected results are evidence that the claims are not obvious. According to the Examiner in the Advisory Action, "patients with trophoblastic disease are known to produce levels of hyperglycosylated hCG and hCG and one of ordinary skill in the art would expect that using two markers for the detection of an assay would be more sensitive and provide greater confirmation than the detection of one marker. Appellants respectfully traverse this assertion. As stated in Cole (page 314, second and third full paragraphs), using hCG to diagnose choriocarcinoma gave a high incidence of false positive results (which can lead to unnecessary treatment, including surgery and chemotherapy). Given this unsuccessful use of hCG alone to diagnose trophoblastic disease, Appellant submits that it would not be obvious to one of skill in the art to combine it in an assay for another marker of tropoblast disease, for example, hyperglycosylated hCG. Appellant submits that it would not have been obvious to one of skill in the art to use two different antibodies, one for hyperglycosylated hCG and one for hCG, because one of skill in the art could not have expected that using an antibody to hCG would increase the sensitivity of an assay for hyperglycosylated hCG as a diagnostic test for trophoblastic disease.

For all of the foregoing reasons, the rejection of claims 23-25 and 42-44 under 35 U.S.C. § 103(a) as being unpatentable over Cole in view of O'Connor in light of Birken in view of Hochstrasser and Birken is clearly improper, and should be reversed.

Appellant further submits that because claim 44 depends from independent claim 23, and because claim 23 is unobvious, as discussed above, claim 44 is similarly unobvious. Accordingly, Appellant submits that the rejection of claim 44 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Cole in view of O'Connor in light of Birken 2001 in view of Hochstrasser and Birken '416, and further in view of Campbell is clearly improper, and should be reversed.

Respectfully submitted,



Jennifer K. Rosenfield
Attorney for Appellant
Reg. No. 53,531

12/22/06
December 22, 2006
Irvine, CA 92618
949-450-1750

APPENDIX A (37 CFR 1.192 (c)(7))

The text of the claims on appeal are:

23. A method for detecting a trophoblastic disease in a subject comprising the steps of:

contacting a biological sample obtained from a subject with a first antibody that specifically binds hyperglycosylated human chorionic gonadotropin and a different second antibody that specifically binds human chorionic gonadotropin, in one assay;

determining an amount of hyperglycosylated human chorionic gonadotropin present in the biological sample;

determining an amount of human chorionic gonadotropin present in the biological sample;

confirming that the subject is not pregnant;

comparing the determined amount of hyperglycosylated human chorionic gonadotropin present in the sample to a 50th percentile of amounts of hyperglycosylated human chorionic gonadotropin present in samples obtained from subjects who do not have a trophoblastic disease; and

comparing the determined amount of human chorionic gonadotropin present in the sample to a 50th percentile of amounts of human chorionic gonadotropin present in samples obtained from subjects who do not have a trophoblastic disease,

wherein an amount of hyperglycosylated human chorionic gonadotropin and an amount of human chorionic gonadotropin present in the sample which is greater than the 50th percentile of the amounts of hyperglycosylated human chorionic gonadotropin and human chorionic gonadotropin present in the samples obtained from subjects who do not have a trophoblastic disease, respectively, indicates the presence of a trophoblastic disease.

24. The method of claim 23, wherein the trophoblastic disease is a choriocarcinoma.

42. The method of claim 23, wherein the sample is selected from the group consisting of liquid samples, and tissue samples.

43. The method of claim 23, wherein the determining step comprises detecting a signal produced by a label.

44. The method of claim 43, wherein the signal is a chemiluminescent signal.

APPENDIX B – Evidence Appendix

No evidence, apart from the file history of the subject application and any evidence entered during the prosecution of said application before the Examiner, has been entered and relied upon in this appeal.

APPENDIX C – Related Proceedings Appendix

As noted on page 1 of this appeal brief, there are no related proceedings respective to the subject application.